

## REMARKS

Applicants have amended claim 1. This amendment is supported by the specification at page 7 and original claim 1. Applicants have also added new claim 16. This amendment is supported by the specification at page 7. As such, these amendments do not constitute new matter and their entry is respectfully requested.

Applicants appreciate the Examiner's withdrawal of the previous rejections.

Claims 1-7 were rejected under 35 U.S.C. §102(b) as being anticipated by Feldman, et al. (U.S. Patent No. 5,665,754).

Applicants respectfully submit that this rejection should be withdrawn for the following reasons.

The Examiner has contended that Feldman allegedly teaches that certain specific inhibitors of PDE-IV can be used to treat "inflammatory diseases and other diseases involving elevated levels of cytokines". There is nothing in Feldman that requires selecting (providing) a patient with CLL. Moreover, the Examiner has cited nothing that in any way suggests that the skilled artisan considers CLL such a disease. As the present specification explains at page 1, lines 15-21, CLL is a **neoplasm** in which a clonal expansion of small lymphocytes accumulate in the marrow, lymph nodes, blood, spleen, liver and sometimes other organisms. This can be contrasted with Feldman's teaching of what it means by an inflammatory disease and a disease with elevated cytokine expression is. When one looks at Feldman and compares it with the definition of CLL, it is clear that CLL is not among the conditions considered (See e.g. col. 34, line 47 – col. 35, line 25). For example Feldman at column 2, lines 14-37, discusses the various diseases that are included stating:

Inflammatory cell activation and excessive or unregulated cytokine (e.g., TNF $\alpha$  and IL-1 $\beta$ ) production are implicated in allergic, autoimmune or inflammatory diseases or disorders, such as rheumatoid arthritis, osteoarthritis, gouty arthritis, spondylitis, sepsis, septic shock, endotoxic shock, gram negative sepsis, gram positive sepsis, toxic shock syndrome, asthma, chronic bronchitis, allergic rhinitis, allergic conjunctivitis, vernal conjunctivitis, eosinophilic granuloma, adult respiratory distress syndrome, chronic pulmonary inflammatory disease, silicosis, pulmonary sarcoidosis, reperfusion injury of the myocardium, brain or extremities, fibrosis, cystic fibrosis, keloid formation, scar formation, atherosclerosis, transplant rejection disorders such as graft vs. host reaction and allograft rejection, chronic granulonephritis, lupus, inflammatory bowel disease such as Crohn's disease and ulcerative colitis and inflammatory dermatoses such as atopic dermatitis, psoriasis or urticaria. Other conditions characterized by elevated cytokine levels include cachexia, cachexia secondary to infection or malignancy, cachexia secondary to acquired immune deficiency syndrome (AIDS), ARC (AIDS related complex), fever and myalgias due to infection, cerebral malaria, osteoporosis and bone resorption diseases, keloid formation, scar tissue formation or pyrexia.

Feldman explicitly explains at column 34, lines 47 to column 35, line 25, what these terms mean. For example, specifically stating that the term inflammatory disease is intended to mean a disease in which an excessive or unregulated inflammatory response leads to excessive inflammatory symptoms, tissue damage, or loss of tissue function. Thus, it is clear to the skilled artisan that, when one looks at Feldman, it is not discussing treating the same type of disease as claimed herein. Further, as discussed above, nothing in Feldman teaches specifically selecting/providing patients with CLL for treatment.

As explained by the U.S. Court of Appeals for the Federal Circuit in *Perricone v. Medicis Pharmaceutical Corporation*, 432 F.3d 1368, 77 U.S.P.Q.2d 1321 at 1378, one can claim a new process over an older process.:

**New uses of old products or processes are indeed patentable** subject matter. See 35 U.S.C. §101 (2000) (identifying as patentable “any new and useful improvements” of a process, machine, manufacture, etc.); *In re King*, 801 F.2d 1324, 1326 (Fed. Cir. 1986) (principles of inherency do not prohibit a process patent for a new use of an old structure.) [Emphasis added]

Thus, the Court found that a method of applying a product to a sunburn is not analogous to a method for applying that product to the skin generally. *Id.*

Accordingly, Applicants respectfully submit that claim 1 and the other claims are not in any way anticipated because these claims are directed to a select patient population, namely those individuals who have been diagnosed as having CLL. Applicants have amended claim 1 to make more explicit that providing a patient having symptoms of CLL as part of the method means that one is specifically selecting such a patient and there is nothing in Feldman that in any way teaches such selection/providing step. Accordingly, there is no anticipation and this rejection of the claims should be withdrawn.

Claims 1-7 were also rejected under 35 U.S.C. §103(a) as being unpatentable over Feldman, et al. in view of Tangye, et al.

As discussed above, the contents of which are incorporated herein, Feldman does not in any way teach or suggest that CLL is an inflammatory disease or a disease associated with elevated levels of cytokines. Tangye does not state otherwise. Rather, the Examiner is applying Tangye because it discusses culturing cells in vitro and allegedly teaches that the cells in vitro may last longer because the cytokines prevent apoptosis in vitro. There is nothing in Tangye that would suggest that in vivo it is the excessive or unregulated production of cytokines, which is responsible for CLL. Indeed, the Examiner’s conclusion that the “prior art” provides a nexus between PDE type IV inhibition (which would lead to a decrease in cytokine production) and B-CLL (wherein cytokines suppress apoptosis of B-CLL cells) is not supported. Indeed, when one looks at the examples presented herein, the mechanism that the Examiner is suggesting is not what Applicants demonstrate is occurring in the CLL cells. The PDE-IV inhibitors are not acting

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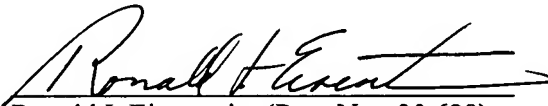
on cytokines in adjacent cells. Rather, they are directly acting on the CLL cells themselves and inducing apoptosis in those cells. Accordingly, this shows that the basis of the rejection is wrong. Further, as discussed above, Feldman does not teach or suggest the invention and Tangye does not overcome the deficiency. Accordingly, the rejection should be withdrawn.

In view of the foregoing, Applicant respectfully submits that all claims are in condition for allowance. Early and favorable action is requested.

In the event that any additional fees are required, the PTO is authorized to charge our Deposit Account No. 50-0850.

Respectfully submitted,

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